L3 ANSWER 9 OF 14 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-100868 [12] WPIDS
DNC C1994-046459
TI New glycolated, glycosylated macromolecule derivs. - esp. polypeptide(s), having **reduced immunogenicity** without redn. of biological activity.
DC B04
IN MTIMKULU, T
PA (BERL-N) BERLEX LAB INC
CYC 19
PI WO 9405332 A2 19940317 (199445)* EN 22p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9350981 A 19940329 (199430)
WO 9405332 A3 19940414 (199516)
ADT WO 9405332 A2 WO 1993-US8196 19930901; AU 9350981 A AU 1993-50981 19930901; WO 9405332 A3 WO 1993-US8196 19930901
FDT AU 9350981 A Based on WO 9405332
PRAI US 1992-937779 19920901
AB WO 9405332 A UPAB: 19940510
A glycolated, glycosylated macromolecule (I) contg. a glycol (GL) bonded to a macromolecule (MM) through a **glycosylation** moeity is new.

GL is pref. a polyalkylene glycol, esp. polyethylene glycol (PEG).

Pref. (I) is of formula -GL-DM-MM (Ia) or GL-O-CO-NH-Alk-N=CH-MM (Ib); DM = diamine bonded to MM through a carbohydrate moiety, forming a Schiff base linkage; Alk - 1-20C alkylene.

USE/ADVANTAGE - MM is specifically a pharmacologically active cpd., pref. a nucleic acid, lipid or polypeptide (pref. a protein (esp. TAb-250 or BACh-250), cytokine, receptor, antithrombotic, growth factor, angiohypertensive reagent, immunoglobulin, interferon, receptor tyrosine kinase, thrombomodulin, transforming growth factor to endothielin). MM typically have enzymatic or peptide hormone activity. TAb-250 and BACh-250 are monoclonal antibodies useful in cancer therapy. (I) usually have the same activity as MM; and may be diagnostic reagents, test samples, etc. as well as therapeutic agents. (I) have undiminished (or even increased) bioactive half-life in a host, **reduced immunogenic** side-effects, increased aq. solubility, increased resistance to proteolytic digestion and/or decreased affinity for formulation polymers as compared with MM (glycosylated but not glycolated). Immunogenicity of MM is reduced while maintaining the biological activity.

L3 ANSWER 7 OF 14 MEDLINE DUPLICATE 2
AN 1998062985 MEDLINE
DN 98062985
TI Branched O-linked oligosaccharides ectopically expressed in transgenic mice reduce primary T-cell immune responses.
AU Tsuboi S; Fukuda M
CS Glycobiology Program, La Jolla Cancer Research Center, Burnham Institute, CA 92037, USA.
NC R37CA33000 (NCI)
SO EMBO JOURNAL, (1997 Nov 3) 16 (21) 6364-73.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
EW 19980302
AB Core 2 beta-1,6-N-acetylglucosaminyltransferase, C2GnT, is a key enzyme in
O-linked oligosaccharide (O-glycan) biosynthesis and the resultant core 2 branch serves as a backbone for additional **glycosylation** to form oligosaccharide ligands such as sialyl Le(x). Since the expression of C2GnT is highly regulated during T-cell development and increases in pathological conditions such as the Wiskott-Aldrich syndrome, we have generated transgenic mice overexpressing C2GnT in the T-cell lineage. Surprisingly, T lymphocytes in the transgenic mice develop normally, but they exhibit a **reduced immune** response when assayed by delayed-type hypersensitivity, proliferation upon stimulation and cytokine
production. Moreover, T lymphocytes from the transgenic mice adhere much less efficiently to ICAM-1 and fibronectin than do T lymphocytes from non-transgenic mice. These results indicate that overexpression of the core 2 branched O-glycans in T lymphocytes results in **reduced immune** responses due to impaired cell-cell interaction. Such an impaired immune response may be one of the causes for immunodeficiency in

L3 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
AN 1998:1508 CAPLUS
DN 128:87876
TI Anti-tumor humanized antibodies with **reduced immunogenicity**
IN Graves, Scott S.; Reno, John M.; Mallet, Robert W.; Hylarides, Mark D.; Searle, Stephen M. J.; Henry, Andrew H.; Pedersen, Jan T.; Rees, Anthony R.
PA Neorx Corporation, USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746589	A2	19971211	WO 1997-US10074	19970606
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 909277	A2	19990421	EP 1997-931103	19970606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-660362 19960607
WO 1997-US10074 19970606

AB The present invention discloses chimeric antibodies, and fragments derived therefrom, which bind to the same tumor antigen recognized by the NR-LU-13 antibody. Pre- and post-translational modification of the chimeric antibodies to prevent immunogenicity of O-linked and N-linked carbohydrate is disclosed. In addn., conjugates contg. such antibodies, and their use in pretargeting methods and conventional antibody therapy and

L3 ANSWER 3 OF 14 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-365606 [31] WPIDS
DNC C2000-110468
TI Novel method for producing glycosylated proteins having reduced allergenicity which are useful in industrial, food, and pharmaceutical preparations.
DC B04 C06 D16
IN ERNST, S; OLSEN, A A; ROGGEN, E L
PA (NOVO) NOVO NORDISK AS
CYC 89
PI WO 2000026354 A1 20000511 (200031)* EN 74p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 9960786 A 20000522 (200040)
ADT WO 2000026354 A1 WO 1999-DK540 19991012; AU 9960786 A AU 1999-60786 19991012
FDT AU 9960786 A Based on WO 200026354
PRAI DK 1999-1419 19991004; DK 1998-1401 19981030; DK 1998-1551 19981125; DK 1999-682 19990517
AB WO 200026354 A UPAB: 20000630
NOVELTY - The method is used to select a glycosylated protein variant which has reduced allergenicity in animals, as compared to a parent protein.

DETAILED DESCRIPTION - A novel method of producing a glycosylated protein variant (PV) having reduced allergenicity in animals, including man, as compared to a parent protein (PP), comprises:

(a) constructing a DNA molecule encoding the PV, the DNA having at least one sub-sequence encoding an additional **glycosylation** site compared to the PP, resulting in a glycosylated PV having allergenicity which is at least 50% lower than the allergenicity of the PP, expressed as the levels of IgE antibody (Ab) response in animals exposed intratracheally;

(b) introducing the DNA molecule into a suitable host capable of **glycosylation**;

(c) culturing the host cell in a suitable medium, whereby the PV is expressed and glycosylated in the host; and

(d) recovering the glycosylated PV from the medium.

INDEPENDENT CLAIMS are also included for the following:

(1) a glycosylated PV having at least a 50% reduction in allergenicity, expressed as the level of IgE antibody response in animals, as compared to the allergenicity of the PP, comprising at least one additional **glycosylation** site, were the glycosylated PV exhibits substantially the same functionality as the PP;

(2) a composition comprising the PV of (1);

(3) use of the composition of (2) for the production of a pharmaceutical, or for the production of a detergent composition or a personal care product;

(4) a DNA construct comprising a DNA sequence encoding the PV of (1);

(5) an expression vector comprising the DNA construct of (4);

(6) a host cell which is capable of expressing a polypeptide, comprising the construct of (4) or vector of (5); and

(7) a method for producing a polypeptide, comprising culturing the

host cell of (6) in a suitable culture medium to obtain expression and secretion of the glycosylated protein into the medium, followed by recovery and isolation of the protein from the culture medium.

USE - The methods are used to select protein variants which have **reduced immunogenicity**, as compared to a parent protein. The selected proteins can be enzymes (especially selected from glycosyl hydrolases, carbohydrases, peroxidases, proteases, lipases, phytases, polysaccharide lyases, oxidoreductases, transglutaminases, and glycoseisomerases (all claimed)), or biological proteins (e.g. insulin, glucagon, pigmentary hormones, somatotropin, erythropoietin, luteinizing hormone, chorionic gonadotropin, relaxin, prolactin, and other peptide hormones). They can be used in industry, housekeeping and/or medicine, e.g. proteins used in personal car products (e.g. shampoo, soap, skin lotions, face creams, cleaning preparations for contact lenses, oral and dental cleaning), hair dyes, toothpaste, food (e.g. in the baking industry), detergents (e.g. dish washing preparations), and pharmaceuticals.

ADVANTAGE - The methods are used to select low allergenic proteins which can be used to prevent cases of allergy in susceptible individuals.

DESCRIPTION OF DRAWING(S) - The figure shows the integrated antibody response in IT-rat model.

Dw